REMARKS:

Claim Objections

Claim 28 was objected to because of the typographical error of "^{111}At" rather than "^{211}At".

Claim 28 was amended to correct the typographical error.

Claim Rejections – 35 USC § 112

Claims 17, 21-28, 32, 33 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing ro particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that claim 17 is vague and indefinite because the word "unrelated" is unclear.

Claim 17 relates to a method for treating chronic lymphocytic leukemia (CLL) in a mammalian subject comprising administering to said subject an effective amount of an isolated monoclonal antibody that **specifically binds** to a polypeptide comprising the sequence set forth in SEQ ID NO: 4, and does not react **detectably** with polypeptides **unrelated** to SEQ ID NO: 4. The word "unrelated" is used in conjuction with the terms "detectably" and "specifically binds". Attention is invited to page 26 of the specification lines 24 to page 27 line 5. The specification defines "specifically binds" to mean an antibody binding at a **detectable** level (within, for example, an ELISA) with the peptide, and does not react **detectably** with **unrelated** peptides. In this context two compounds are said to "bind" when the binding constant for complex formation exceeds about 10^3 L/mol. Thus unrelated to SEQ ID NO:4 means anything petptide that the antibody binds with less than 10^3 L/mol affinity.

Claim Rejections – 35 USC § 102

Claims 17, 21-23, 32, 33 and 54 are rejected under 35 U.S.C. 102(b) as breing anticipated by Schneider et al (WO 01/24811). The Examiner says that Schneider et al disclose a method for treating a mammaliam subject with a cancerous disorder, wherein said

cancers express APRIL receptor or APRIL comprising the administration of anti-APRIL Receptor antibodies (page 4, lines 17-21 and page 16, lines 24-32), and Schneider et al disclose examples of such cancers as including CLL (page 16, line 33-34 and page 18 line 12).

It is respectfully submitted that Applicants whole heartedly disagree with Examiner's reading of Schneider. At the outset, page 4, lines 17-21 of Schneider states

> *...APRIL-antagonists, including for example, anti-APRIL-R antibodies, may be used in the treatment of subjects at risk of developing cancer*

Examiner is reminded that instant claims are directed to the treatment of CLL for patients who already have CLL, and not to treatment of subjects at risk of developing cancer. Secondly, disclosure of Schenider on page 16 is very vague. There are literally hundreds of types of cancers known to man, and it does not specifiy any which ones.

Pages 16-18 of Schneider is of no help either. One can see CLL listed on page 18, line 12. But upon close reading of Schneider on page 17, it appears that the table is a type of cells that one can detect some level of expression of APRIL. It does not give any idea of what expression level is .i.e. low? medium? high? only barely detectable? Page 17, line 1-2 of Schneider says only when BCMA is highly expressed would be candidates.

The following is excerpts from MPEP 2121.01

"In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... ." In re Hoeksema, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Elan Pharm., Inc. v. **>Mayo Found. For Med. Educ. & Research<, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003) (At issue was whether a prior art reference enabled one of ordinary skill in the art to produce Elan's claimed transgenic mouse without undue experimentation. Without a disclosure enabling one skilled in the art to produce a transgenic mouse without undue experimentation, the reference would not be applicable as prior art.). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Furthermore, it is well known that antibody can be agonistic or antagonistic. Schneider provides no guidance how to make antagonistic antibody over agnostic antibody either.

It should be reminded that it was Applicants who generated data showing that BCMA (ly1732P) is over expressed in both CLL and multiple myeloma. Applicants generated a monoclonal antibody to BCMA referred to as 44C1. The specification shows that this antibody binds to BCMA. This is exemplified by using H929, (a multiple myeloma cell line), as shown by Flow cytometry (Figure 3). The BCMA specific antibody has a binding affinity of 58pM as shown using the Biacore T100 (Figure 2) and has a clear biological activity in treating human tumours as can be seen by the data in Figure 4 which shows that upon binding to BCMA the antibody enables ADCC killing of the multiple myeloma cells by NK cells in vitro.

For the above reasons, it is believed that Applicants successfully overcame Schneider.

Claim Rejections – 35 USC § 103

Claims 17, 21-23, 26, 27, 33 and 54 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al (WO 01/24811) in view of Hanna et al (U.S. 2002/0028178).

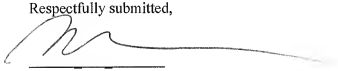
Further Claims 17, 21-25, 33 and 54 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al in view of Shadidi et al.

For the same reason as stated above, Applicants believe that Schenider is effectively removed as a reference as not teaching or enabling that antibody to APRIL can be used to treat existing CLL; thus, Applicants believe all the claims are now allowable.

Applicants believe they have adequately addressed the issues raised by the Examiner. Re-examination and allowance of the application are earnestly requested. Should the

Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper the Commissioner is hereby authorized to charge Deposit Account No. 19-2570, accordingly.

Respectfully submitted,



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